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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,791	04/25/2001	David Russell Blake	9374.21USWO	3690

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MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER
WEBER, JON P

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 02/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/763,791	BLAKE ET AL.	
	Examiner	Art Unit	
	Jon P. Weber, Ph.D.	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *19-31,36 and 37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 32-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4, 5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Status of the Claims

Claims 1-37 have been presented for examination.

Election/Restriction

Applicant's election with traverse of Group I, claims 1-18 and 32-35 in Paper No. 9, filed 04 December 2001 is acknowledged. The traversal is on the ground(s) that Applicants do not want to be bound by Examiner's reasoning. This is not found persuasive because the response has not rebutted the basis of the restriction with any evidence or facts.

The requirement is still deemed proper and is therefore made FINAL. Claims 19-31 and 36-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions Group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

Specification

The attempt to incorporate subject matter into this application by reference to Biozyme product literature at page 15, lines 24-26, is improper because the specific activity of the xanthine oxidase (U/μg) used in the examples is critical to relating the μg/ml claimed to the U/ml normally reported for enzymes, U/ml ÷ U/μg = μg/ml.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 32 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 32 is drawn to the XOR composition of Example 1.

In example 1, at lines 18-21 the critical description is provided.

To the "milk" bijou were added either 598 µl Cow and Gate formula feed and 2 µl XOR or 100 µl buttermilk and 500 µl 1X PBS to give a total volume in the "milk" bijou of 600 µl in each case.

The amount of XOR in either µg or activity units that is being added is unclear. The volume of the "bijou" is unknown, although 600 µl of mixture is added to it. Accordingly, the concentration of XOR in the bijou cannot be determined from the information directly presented in the Example.

One might guess that there is 1 ml of pasteurized milk in the bijou (by analogy to page 25, lines 27-29) giving a total volume of 1.6 ml. One can guess that the XOR stock is 10.7 mg/ml (page 15, lines 24-26). Assuming these two guesses are correct, the concentration of XOR in the bijou is: 2 µl x 10.7 mg/ml ÷ 1.6 ml = 13.375 µg/ml.

There is also a XOR-containing buttermilk sample in this Example. It is not clear if this or the other formula feed is being claimed.

Applicants are required to clarify this Example, so the metes and bounds of the claim can be determined.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 and 32-35 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (and others) recites "active xanthine oxidase" which is vague and indefinite because the degree and magnitude of the "activity" of the xanthine oxidase is unclear. If a given sample of enzyme has low specific activity it is still active, but more μg of sample will be needed to achieve a desired level of activity, U/μg x μg = U, as compared to a higher specific activity sample.

Claims 11-15 recite "A combination product" which is not art-accepted terminology. This is a kit if it comprises two or more products separately packaged.

Claim 11 recites "substantially no active XOR" which is vague and indefinite because the metes and bounds of the amount of XOR is not clear and no clear definition can be found in the disclosure.

Claim32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. This claim is an omnibus type claim.

Claims 33-35 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the amount of xanthine oxidase to include in the

formulation so as to obtain the functional intended use. Absent this limitation it is assumed that any amount is sufficient.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-10 and 33-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Björck et al. (1979).

Björck et al. (1979) disclose that the concentration of xanthine oxidase normally in milk is 120 μg/ml (page 1213). In table 3, the effect of concentrations of more than 50 μg/ml of xanthine oxidase in synthetic medium (paragraph bridging pages 1211-1212) on *E. coli* 9703 viability is reported.

Claims 1, 7-8, 10-16, 18 and 33-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Cooray et al. (1995).

Cooray et al. (1995) disclose the effect of added xanthine oxidase to milk and phosphate synthetic medium on the viability of several bacteria in Table 3. The concentration of added enzyme is 2.5 or 5 μg/ml.

Claims 1-4, 6-11, 14-17 and 33-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Clark et al. (1976).

Clark et al. (1976) disclose a food supplement for rats which is pasteurized and homogenized half cream/half milk (H/H) which contains 0.04 U/ml of xanthine oxidase and which is supplemented with xanthine oxidase at 0.16 U/ml, giving a combined 0.20 U/ml (page 888, Methods). Assuming that the specific activity of xanthine oxidase is 0.1-0.4 U/mg (Sigma Type IV, see addendum), this corresponds to 500-2000 μg/ml. Clearly the amount of xanthine oxidase is more than physiological because the sample is supplemented. Saline supplemented with 0.16 U/ml was also used (corresponds to 400-1600 μg/ml).

Claims 1-4, 7, 11 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Saugstad et al. (1988).

Saugstad et al. (1988) disclose a physiological saline solution comprising xanthine oxidase at 0.5-1.0 U/ml (Table I). Since the xanthine oxidase is 0.4 U/mg (Chemicals, page 63), this corresponds to 600-1250 μg/ml.

Claims 1-17 and 33-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Ho et al. (1978).

Ho et al. (1978) disclose a food supplement for rats and chicks which is pasteurized and homogenized half cream/half milk (H/H) fortified with 0.015 volumes of Sigma Grade IV xanthine oxidase (0.22 U/ml, page 56), 0.0075 volumes of detergent and 1.0 volumes of corn oil. The amount of xanthine oxidase is 0.22 U/ml of 0.1-0.4 U/mg corresponding to 2.2-0.55 mg/ml.

Taking 1.0 volumes as 1.0 ml, for convenience, this corresponds to 2.0225 ml total. Hence the fortification with xanthine oxidase corresponds to 0.015 x (0.55 to 2.2) ÷ 2.0225 = 1 to 4 μg/ml). Taking the known value of naturally occurring xanthine oxidase of 120 μg/ml (*vide supra*, Björck et al., 1979) the amount of xanthine oxidase is greater by a small amount over that naturally occurring.

Claims 1-10 and 33-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Zikakis (US 4,238,566).

Zikakis (US 4,238,566) discloses that the naturally occurring amount of xanthine oxidase in whole milk is about 0.034 U/ml (Table 1). Taking the specific activity of xanthine oxidase in Sigma Type IV xanthine oxidase (0.1-0.4 U/mg) as a guide, this corresponds to 85-340 μg/ml. This amount of xanthine oxidase in milk is consistent with the 0.04 U/ml reported by Clark et al. (1976) (*supra*).

Claims 1-11, 13-17 and 33-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Antrim et al. (US 4,961,939).

Antrim et al. (US 4,961,939) disclose adding an enzyme-containing stabilizer to edible emulsions containing fish oil to prevent formation of malodorous alcohols and aldehydes (column 1). The stabilizer system (c) contains about 0.01 to 10 U /mg emulsion (~ml), preferably 0.1 to 1.0 units of xanthine oxidase (column 4, lines 5-8). Using Sigma Type IV xanthine oxidase (0.1-0.4 U/mg) as a guide, this corresponds to 25 to 100000 μg/ml, preferably 250 to 10000 μg/ml. In System #4 (column 5, lines 57-64) 100 U of xanthine oxidase Grade III from Sigma at

1.5 U/mg (corresponds to 66.67 mg enzyme) is added to the milk phase of System #2, total volume of about 473.8 ml, giving a final concentration of about 140 µg/ml. Taking the known value of naturally occurring xanthine oxidase of 120 µg/ml (*vide supra*, Björck et al., 1979) the amount of xanthine oxidase is greater than that naturally occurring.

Claims 1, 6-10 and 33-34 are rejected under 35 U.S.C. 102(b) as being anticipated by De Jong et al. (US 5,747,078). N.B. the effective US filing date for the purposes of this statute is the PCT filing date of 27 August 1999.

De Jong et al. (US 5,747,078) disclose adding xanthine oxidase and its corresponding substrate to food products for the purpose of long-term preservation by virtue of the ability of this system to provide controlled slow release of antimicrobial quantities of peroxide. The enzyme is provided in immobilized form as dry particles or liquid to be added to the food product. It can be used with liquid or solid foods (column 6, lines 45-61).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-18 and 32-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Björck et al. (1979), Ho et al. (1978), Clark et al. (1976), Zikakis (US 4,238,566), Antrim et al. (US 4,961,939) and De Jong et al. (US 5,747,078) in view of Reddy et al. (US 5,876,990).

The teachings of Björck et al. (1979), Ho et al. (1978), Clark et al. (1976), Zikakis (US 4,238,566), Antrim et al. (US 4,961,939) and De Jong et al. (US 5,747,078) have been discussed above. Björck et al. (1979), Ho et al. (1978), Clark et al. (1976), Zikakis (US 4,238,566), Antrim et al. (US 4,961,939) and De Jong et al. (US 5,747,078) lack treating Scours or the express composition of Example 1.

Reddy et al. (US 5,876,990) disclose adding peroxide producing enzyme mixture to animal feed products to inhibit the growth of a wide range of microorganisms known to infect farm animals (Example 12). The incidence of Scours and diarrhea were reduced compared to controls which received only feed (i.e., without the added enzymes) (column 30, lines 18-25).

A person of ordinary skill in the art at the time the invention was made would have been motivated to treat Scours with a peroxide producing enzyme composition comprising xanthine oxidase because Reddy et al. (US 5,876,990) disclose that peroxide producing enzymes inhibit the growth of microorganisms that cause Scours and De Jong et al. (US 5,747,078) disclose that xanthine oxidase is a peroxide producing enzyme that inhibits the growth of microorganisms. A number of the references of record establish that it is well-known in the art that xanthine oxidase, especially in combination with its substrate, has antimicrobial properties. The amounts of xanthine oxidase found in milk are thought to be a major contributor to maintaining the sterility of milk and colostrum. The naturally occurring amount in milk is shown to be about 0.04 U/ml corresponding to about 120 μg/ml of Grade IV xanthine oxidase from Sigma. A number of references suggest that antimicrobial enzymes can be added to animal feed to enhance the health of the animals. Hence, it is reasonably expected that the same antimicrobial benefits that accrue to milk products containing xanthine oxidase will transfer to other animal feeds or formulas.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add antimicrobial quantities of xanthine oxidase to animal or human feed formulations.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon P. Weber, Ph.D. whose telephone number is 703-308-4015. The examiner can normally be reached on daily, off 1st Fri, 9/5/4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jon P. Weber, Ph.D.
Primary Examiner
Art Unit 1651

JPW
February 13, 2002